"DESIGN AND DEVELOPMENT OF COLON TARGETED DRUG DELIVERY SYSTEM"

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1. INTRODUCTION

1. Introduction

During the past decades research is going on in developing the methods to target the drug to the specific region. The goal of targeted drug delivery is to deliver the drug to the specific organ. Colon targeted drug delivery is used to deliver the substances that are degraded by the digestive enzymes in the stomach such as proteins and peptides. It is also used for the treatment of various diseases like ulcerative colitis, crohn's disease, intestinal cancer, diarrhoea, for the treatment of diseases sensitive to circadian rhythms like Asthma, Angina, for the delivery of steroids, etc. colon targeted drug delivery of drugs reduces the systemic side effects. Colon targeted drug delivery system increases the absorption of poorly absorbable drugs due to the high retention time of the colon During the past decades research is going on in developing the methods to target the drug to the specific region. The goal of targeted drug delivery is to deliver the drug to the specific organ. Colon targeted drug delivery is used to deliver the substances that are degraded by the digestive enzymes in the stomach such as proteins and peptides. It is also used for the treatment of various diseases like ulcerative colitis, crohn's disease, intestinal cancer, diarrhoea, for the treatment of diseases sensitive to circadian rhythms like Asthma, Angina, for the delivery of steroids, etc. colon targeted drug delivery of drugs reduces the systemic side effects. Colon targeted drug delivery system increases the absorption of poorly absorbable drugs due to the high retention time of the colon (Danda S, 2013).

1.1 Advantages **(Danda S, 2013)**

1. Used for the effective treatment of inflammatory bowel diseases like ulcerative colitis, crohn's disease, etc.
2. Decreases the side effects in the treatment of colon diseases.
3. Prevents gastric irritation resulting due to the administration of NSAIDs.
4. Minimizes first pass metabolism.
5. Provides suitable environment for proteins and peptides that are sensitive to gastric fluid and digestive enzymes.
6. Increased patient compliance.

7. Decreased frequency of administration hence decreased cost of drugs.
8. High retention time thus increasing the bioavailability of poorly absorbable drugs.

1.2 Limitations **(Danda S, 2013)**

1. Multiple manufacturing steps.
2. Incomplete release of drug.
3. Lowering of bioavailability due to binding of drugs to intestinal contents

1.3 Factors affecting colon targeted drug delivery **(Danda S, 2013).**

1. Physiological factors
2. Pharmaceutical factors

1. Physiological factors

a. Gastric emptying

Drug delivery to the colon upon oral administration depends mainly on gastric emptying and bowel transit time. Upon reaching the colon the transit time of dosage form depends on the size of the particles. Smaller particles have more transit time compared to larger particles. Diarrhoea patients have shorter transit time whereas constipation patients have longer transit times.

b. pH of colon

The pH of GIT varies between different individuals. The food intake, diseased state, etc. influences the pH of the GIT. This change in the pH in different parts of GIT is the basis for the development of colon targeted drug delivery systems. Coating with different polymers is done to target the drug to the site.

c. Colonic microflora and enzymes

The GIT contains a variety of microorganisms that produces many enzymes need for metabolism. Growth of this microflora is controlled by the GIT contents and peristaltic movements. The enzymes released by different microorganisms E. coli, Clostridia, Lactobacilli, Eubacteria, Streptococci are responsible for the various metabolic reactions that take place in the GIT.

2. Pharmaceutical factors

a. Drug candidates:

Due to high retention time of colon, colon causes an increase in the absorption of poorly absorbed agents like peptides, etc. drugs used for treatment of inflammatory bowel diseases, etc. are suitable for colon targeted drug delivery system.

b. Drug carriers:

The selection of carrier for CDDS depends on the nature of the drug, disease for which the drug is used. the various physicochemical factors of drug that effect the carrier selection includes chemical nature, stability, partition coefficient, functional groups of drug molecule, etc.

1.4 DRUGS SUITABLE FOR CDDS (Sateesh KV, 2009)

Based on literature review, the following different categories of drugs are suitable for colon drug delivery.

- Drugs used to treat irritable bowel disease (IBD) require local delivery at drug to colon e.g. sulfasalazine, olsalazine, mesalazine, steroids like fludrocortisone, budesonide, prednisolone and dexamethasone.
- Drugs to treat colonic cancer require local delivery e.g. 5-fluorouracil, doxorubicin, and methotrexate.
- Protein and peptide drugs - eliminating drug degradation e.g. growth hormones, calcitonin, insulin, interleukin, interferon and erythropoietin.
- To treat infectious diseases (amoebiasis & helminthiasis) - requires site specific delivery e.g. metronidazole, mebendazole and albendazole.
- To treat rheumatoid arthritis (NSAIDS), nocturnal asthma, angina require delay in absorption due to circadian rhythms
- Drugs showing more selective absorption in colon than small intestine due to small extent of paracellular transport e.g. glibenclamide, diclofencac, theophylline, ibuprofen, metoprolol, and oxyprenolol.

1.5 NEED OF COLON TARGETED DRUG DELIVERY (Prathap M, 2014)

- Targeted drug delivery to the colon would ensure direct treatment at the disease site, lower dosing and fewer systemic side effects.
- Site-specific or targeted drug delivery system would allow oral administration of peptide and protein drugs, colon-specific formulation could also be used to prolong the drug delivery.

- The colon is a site where both local or systemic drug delivery could be achieved, topical treatment of inflammatory bowel disease, e.g. ulcerative colitis or Crohn's disease. Such inflammatory conditions are usually treated with glucocorticoids and sulphasalazine (targeted).
- A number of others serious diseases of the colon, e.g. colorectal cancer, might also be capable of being treated more effectively if drugs were targeted to the colon.
- Formulations for colonic delivery are also suitable for delivery of drugs which are polar and/or susceptible to chemical and enzymatic degradation in the upper GI tract, highly affected by hepatic metabolism, in particular, therapeutic proteins and peptides.

1.6 Criteria for selection of drug for colonic drug delivery **(Ratnaparkhi MP, 2013)**

- **Drug candidate**

Drugs which show poor absorption from the stomach as intestine including peptide are most suitable for CDDS. The drug used in treatment of IBD, ulcerative colitis, diarrhoea and Colon cancers are ideal candidates for local colon delivery.

- **Drug carrier**

The selection of carrier for particular drug candidate depends on the physiochemical nature of the drug as well as the disease for which the system is to be used. The factors such as chemical nature, stability and partition coefficient of drug and the type of absorption enhancers chosen influence the carrier selection. Moreover, the choice of drug carrier depends on the functional groups of drug molecule. The carriers which contain additives like polymers (may be used as matrices and hydro gels as coating agents) may influence the release properties and efficacy of the systems.

2. LITERATURE REVIEW

2.1 Raghuvanshi NH *et al* (2015) was studied the Matrix tablets of Prednisolone which was prepared by wet granulation method using various proportions of Sterculia gum with Carbopol 934P and Sterculia gum with Ethyl cellulose at 1:1, 1: .5 and 1:2 ratio was used. Coating was carried out by using 1:1 ratio of Eudragit L100 and Eudragit S100. All the preparation were evaluated for Pre compressional properties, Post compressional properties and in-vitro Dissolution study in different pH buffer of 0.1N HCL ,pH 7.4 , pH 6.8 in order to mimic GIT condition. Formulation shows good results with good percentage yield.

2.2 Prathap M *et al* (2014) was studied the colon: targeted drug delivery system – a review. It have a discussion on introduction of colon, need and approaches of colonic drug delivery, factor effecting colonic transition, colonic diseases and the novel and emerging technologies for colon targeting.

2.3 Dangi AA *et al* (2013) was studied the colon specific sustained release tablet using levetiracetam (LEV), microbially degradable polymeric carrier (pectin), coating material and matrix forming polymers. The colon targeted tablet was prepared by wet granulation technique using different percentage of pectin as matrix carrier, starch mucilage as a binding agent, HPMC K-100 as swellable polymer and coated with Eudragit polymers. Pectin, drug and physical mixture were evaluated for incompatibility study by Fourier transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC). All the batches of matrix tablet (F1-F4) were subjected for in-vitro dissolution in various simulated gastric fluids for suitability for colon specific drug delivery system. Tablets were evaluated for micromeritic properties of granules, physical properties, drug content, water uptake and erosion characteristics. F2 was optimized and subjected to coating based on evaluation results. The dissolution study of F2 revealed, in simulated intestinal fluid (SIF) release was 40.48% at the end of 6h and in simulated colonic fluids (rat caecal content) was 102.88% after degradation at the end of 8h. The colon targeted matrix

tablet of LEV showed no change either in physical appearance, drug content or dissolution pattern after performing stability study for 3 months.

2.4 Singh R *et al* (2012) was studied the colon targeted drug delivery systems for Nitrofurantoin using guar gum as a carrier. Matrix tablets containing various proportions of guar gum were prepared by wet granulation technique using starch paste as a binder. The in-vitro drug release study was undertaken at 37±0.5°C in 0.1N Hcl for 2 hr; followed by pH 7.4 phosphate buffer (3hr) finally in simulated colonic fluid pH 6.8 phosphate buffer containing 4% w/v rat ceacal content for 10 hr. It was found that 10.04% drug is released in first 5hr from F4 (GG-20%), where as the other matrix tablets released 20-30% of Nitrofurantoin in physiological environment of stomach and small intestine. When studies were continued in colonic fluids, matrix tablets released almost 100% drug. The results of the study show that matrix tablets containing 20% of guar gum are most likely to provide targeting of Nitrofurantoin in the colon.

3. AIM AND OBJECTIVE

3.1 Aim

To design and develop colon targeted drug delivery system.

3.2 Objective

- To formulate colon targeted drug delivery system.
- To get Targeted drug delivery to the colon would ensure direct treatment at the disease site
- To get effective drug treatment.
- To get maximum bioavailability.
- To get Site-specific or targeted drug delivery system would allow colon-specific formulation could also be used to prolong the drug delivery.

4. PLAN OF WORK

4.1. Literature survey

4.2. Procurement of Drugs and Excipients

4.3. Preformulation study of drug.

- Determination of bulk density and tapped density
- Compressibility index
- Hausner's ratio
- Angle of repose

4.4 Formulation of colon targeted Tablet.

4.5 Evaluation -

- Tablet thickness
- Hardness
- Weight variation
- Water uptake and erosion study
- Assay for drug content
- *In-vitro* release Study

4.6 Stability Studies

4.7 Results and Discussion

5. REFERENCES

Amish Ashvinkumar Dangi, Ganure Ashok, and Jain Divya, 2013, "Formulation and Evaluation of Colon Targeted Drug Delivery System of Levetiracetam using Pectin as Polymeric Carrier", *Journal of Applied Pharmaceutical Science*, 3(01):078-087.

Danda Sreelatha, Chandan Kumar Brahma,2013, "Colon Targeted Drug Delivery – A Review on Primary and Novel Approaches", *Journal of Global Trends in Pharmaceutical Sciences*, 4(3): 1174-1183.

M. Prathap, MD. Gulshan, N. Rama Rao, 2014, "Colon: Targeted Drug Delivery System – A Review", *International Journal of Research in Pharmaceutical and Nano Sciences.* 3(5): 429 - 437.

Neha Singh Raghuvanshi, Laxmi Goswami, Dr. Preeti Kothiyal, 2015, "Formulation And Evaluation Of Colon Targeted Dosage Form Of Prednisolone Tablet Using Sterculia Gum", *Indian Journal of Drugs*,3(1): 1-4.

Ranjit Singh, 2012, "Formulation and evaluation of colon targeted drug delivery System", *Int. J. of Pharm. & Life Sci.*, 3(12): 2265-2268.

Ratnaparkhi MP., Gupta Jyoti P., Budhavant Kalyani A., 2013, "Colon Targeted Drug Delivery System", *International Journal of Pharma Research & Review*, 2(8):33-42.

Sateesh Kumar Vemula and Prabhakar Reddy Veerareddy, 2009, "Different Approaches To Design And Evaluation Of Colon Pecific Drug Delivery Systems", *Int. Journal Of Pharmacy & Technology*,1(1):1-35.

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